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Theodore A. Wood Elizabeth J. Haanes Bruce E. Chalker Joseph S. Ostroff Frank R. Cottingham Christine M. Lhulier Christine M. Lhuller Rae Lynn Prengaman Jane Shershenovich* Lawrence J. Carroll* George S. Bardmesser Daniel A. Klein* Rodney G. Maze Jason D. Eisenberg Michael D. Specht Andrea J. Kamage Tracy L. Muller* Jon E. Wright* LuAnne M. Yuricek*

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<u>Of Counsel</u> Kenneth C. Bass III Evan R. Smith

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July 25, 2003

WRITER'S DIRECT NUMBER: (202) 772-8525 **INTERNET ADDRESS:** BRIAND@SKGF.COM

Commissioner for Patents PO Box 1450 Alexandria, VA 22313-1450

Via Hand Carry to Examiner Gerald G. Leffers, Jr. Art Unit 1636

Re:

U.S. Utility Patent Application

Appl. No. 09/438,358; Filed: November 12, 1999

For:

Compositions and Method for Recombinational Cloning

of Nucleic Acid Molecules

Inventors:

GERARD et al.

Our Ref:

0942.4640001/RWE/BJD/JKM

RECEIVED

JUL 3 0 2003
TECH CENTER 1600/2900

Sir:

Transmitted herewith for appropriate action are the following documents:

- COURTESY COPY of the postcard receipt dated September 18, 2000, the postcard 1. receipt dated March 8, 2001, the Information Disclosure Statement (IDS), and Form PTO-1449 (62 pages) as originally filed on September 18, 2000, and as filed as a courtesy copy on March 8, 2001;
- SECOND COURTESY COPY of each missing reference cited on Form PTO-1449 2. (38 documents: AT1, AS4, AT4, AR5, AR9, AR19, AT21, AS22, AS24, AS26, AS29, AR32, AS32, AR35, AT36, AS38, AT40, AR46, AS46, AR47, AR49, AS49, AR50, AS52, AR53, AR54, AR57, AT58, and AS59-AS62) as originally filed on September 18, 2000, and as filed as a courtesy copy on March 8, 2001; and
- One (1) return postcard. 3.

Commissioner for Patents July 25, 2003 Page 2

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Brian J. Del Buono

Attorney for Applicants

Registration No. 42,473

RWE/BJD/JKM/acr Enclosures

SKGF_DC1:159399.1

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TECH CENTER 1600/2900

ASFILED Sextender 18,2000

Due Date: Feb. 12, 2000

Art Unit: 1636

Examiner: Leffers, Jr., G.

Docket: 0942.4640001

Atty: RWE/BJD

For: Compositions and Methods for Recombinational Cloning of Nucleic Acid Molecules

.When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

1. Transmittal letter (in duplicate);

Filed:

Applicant:

Application No.:

2. Information Disclosure Statement (in duplicate);

3. 62 pages of Form PTO-1449 citing 234 documents; and

Gerard et al.

09/438,358

November 12, 1999

4. A copy of each of the 234 cited documents.



Please Date Stamp And Return To Our Courier

ASFILED March 9,2001

Due Date: March 8, 2001

Examiner: Leffers, Jr., G.

Docket: 0942.4640001

Atty: RWE/BJD

Art Unit: 1636

[Rule 56 IDS 3/19/01 0942.464PC01]

Applicant: Gerard et al.

Application No.: 09/438,358

Filed: November 12, 1999

. 10000112, 1999

For: Compositions and Methods for Recombinational Cloning of Nucleic Acid Molecules

When receipt stamp is placed hereon, the USPTO acknowledges receipt of the following documents:

1. SKGF Cover Letter (in duplicate);

2. PTO Fee Transmittal Form (PTO/SB/17);

3. Check No. 30592 in the amount of \$290.00 to cover the cost of a one month extension of time for a large entity (\$110.00) and the filing of an Information Disclosure Statement (\$180.00);

4. Petition For Extension of Time Under 37 C.F.R. § 1.136(a)(1) (in duplicate);

5. First Supplemental Information Disclosure Statement and Fee Under 37 C.F.R. § 1.97(c) (in duplicate);

6. 4 pages of Form PTO-1449 citing 21 documents;

7. A copy of each of the 21 cited documents;

8. Courtesy copies of missing documents AT1, AS4, AT4, AR5, AR9, AR19, AT21, AS22, AS24, AS26, AS29, AR32, AS32, AR35, AT36, AS38, AT40, AR46, AS46, AR47, AR49, AS49, AR50, AS52, AR53, AR54, AR57, AT58 and AS59-AS62, cited on Form PTO-1449 with the Information Disclosure Statement filed September 18, 2000:

9. Amendment & Reply Under 37 C.F.R. § 1.111; and

10. Return postcard.

Please Date Stamp And Return To Our Courier

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

GERARD et al.

Appl. No. 09/438,358

Filed: November 12, 1999

For:

Compositions And Methods For

Recombinational Cloning of Nucleic Acid Molecules

Art Unit:

1636

Examiner:

Leffers, Jr., G.

Atty. Docket: 0942.4640001/RWE/BJD

Information Disclosure Statement

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of each of these documents is provided.

The Examiner is also referred to the following commonly owned, co-pending patent applications, which are directed to related technical subject matter:

U.S. Application No. 09/005,476, filed January 12, 1998;

U.S. Application No. 09/177,387, filed October 23, 1998;

U.S. Application No. 09/233,492, filed January 20, 1999;

U.S. Application No. 09/233,493, filed January 20, 1999;

U.S. Application No. 09/296,280, filed April 22, 1999; U.S. Application No. 09/296,281, filed April 22, 1999;

U.S. Application No. 09/432,085, filed November 2, 1999;

U.S. Application No. 09/498,074, filed February 4, 2000;

U.S. Application No. 09/517,466, filed March 2, 2000; and

U.S. Application No. 09/518,188, filed March 2, 2000.

The identification of these U.S. Applications is not to be construed as a waiver of secrecy as to those applications now or upon issuance of the present applications as patents. The Examiner is respectfully requested to consider the cited applications and the art cited therein during examination.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith. It is further understood that the Examiner will consider information that had been cited or submitted to the U.S. Patent and Trademark Office in a prior application relied on under 35 U.S.C. § 120. 1138 OG 37, 38 (May 19, 1992).

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and to indicate in the official file wrapper of this patent application that the documents have been considered.

This Information Disclosure Statement is being filed more than three months after the U.S. filing date but before a first Office Action on the merits. No statement or fee is required.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036. A duplicate copy of this pleading is enclosed.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Brian J. Del Buono Agent for Applicants Registration No. 42,473

Date: September 18, 2000

1100 New York Avenue, N.W. Suite 600 Washington, D.C. 20005-3934 (202) 371-2600

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Page 1 of 62

					ATTY. DOCKET NO. 0942.4640001	PLICATION NO. 9/438,358			
		FORM PTO		·CNT	APPLICANT Gerard <i>et al</i> .				
. <u>I</u>	NFORMATIC	ON DISCL	OSURE STATE	<u>11EN I</u>	FILING DATE November 12, 1999		0UP 36		
				U.S	. PATENT DOCUMENTS			<u> </u>	
AMINER			WA MINDED	DATE	NAME	CLASS	SUB-CLASS	FILING DATE	
ITIAL	-	 	NT NUMBER	06/16/1987	Backman, K.C.	435	68	04/30/1984	
	AA1	4,673,		05/10/1998	Backman et al.	435	108	02/13/1985	
	AB1	4,743,			Sauer B.L.	435	172.3	04/29/1987	
	AC1	4,959,		09/25/1990	Blattner, F.R.	435	6	10/01/1990	
	AD1	5,227		07/13/1993	Auerbach, J.I.	435	91.1	10/15/1993	
	AE1	5,354		10/11/1994		435	172.3	03/15/1994	
	AF1	5,434	,066	07/18/1995	Bebee, R.L., et al.	435	172.3	12/21/1993	
	AG1	5,470	,727	11/28/1995	Mascarenhas et al.	435	91.2	02/03/1995	
	AH1	5,591	,609	01/07/1997	Auerbach, J.I.		91.2	09/26/1995	
	AI1	5,614	,389	03/25/1997	Auerbach, J.I.	435	172.3	01/20/1995	
	AJ1	5,635	,381	06/03/1997	Hooykaas et al.	435			
	AK1	5,658		08/19/1997	Odell et al.	435	172.3	07/27/1994	
	AKT	-7		FORI	IGN PATENT DOCUMENTS				
XAMINER				2175	COUNTRY	CLASS	SUB-CLASS	TRANSLATION	
NITIAL		DOCUM	MENT NUMBER	DATE	COOKIKI			Ye	
	AL1	EP 0	160 571 A2	11/06/1985	Europe			Ye	
	AM1	EP 0	300 422	01/25/1989	Europe			Ye	
	AN1	WO 91	1/02801	03/07/1991	WIPO			Ye	
	A01	WO 9	1/16427	10/31/1991	WIPO			N Ye	
	AP1	WO 9	2/20791	11/26/1992	WIPO			N	
	17,0		OTHER	(Including Auth	or, Title, Date, Pertinent	Pages, etc.)			
	AR	1	Abremski, for A Exci	K., and Gottesm sive Recombinat	an, S., "Purification of th ion," <i>J. Biol. Chem. 257(16</i>	ne Bacteriopha):9658-9662 (1	ge λ xis Gene Pr 982).	oduct Required	
	AS	1	Abremski, Properties	K., and Hoess, of the Cre Red	R., "Bacteriophage P1 Site- combinase Protein," <i>J. Biol</i>	specific Reco Chem. 259:150	mbination - Puri 19-1514 (1984).	fication and	
	АТ	1	Abremski, Topoisomen	K., et al., "Be case Activity o	acteriophage P1 Cre- <i>loxP</i> Sit f the Cre Recombination Pro	te-specific Re tein," <i>J. Biol</i>	combination: Sit . Chem. 261(1):3	e-specific DNA 91-396 (1986).	
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Page 2 of 62

			4440		ATTY. DOCKET NO. 0942.4640001	09/4	ICATION NO.			
	ı	FORM PTO	-1449		APPLICANT Gerard et al.		-1	33 -1		
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AMINER	T	· ·			NAME	CLASS	SUB-CLASS	FILING DATE		
ITIAL			NT NUMBER	DATE	Devine et al.	435	20.1	03/02/1994		
	AA2	5,677,	170	10/14/1997	Wahl et al.	435	325	06/07/1995		
	AB2	5,677,		10/14/1997		530	327	07/29/1996		
	AC2	5,710,	248	01/20/1998	Grose, C.F.	800	208	06/07/1995		
	AD2	5,723,	765	03/03/1998	Oliver et al.	435	6	02/01/1996		
	AE2	5,733,	733	03/31/1998	Auerbach, J.I.	435	320.1	06/10/1996		
	AF2	5,733,	743	03/31/1998	Johnson et al.	435	172.3	03/08/1996		
	AG2	5,744,	,336	04/28/1998	Hodges et al.	435	91.41	12/19/1994		
	AH2	5,766	,891	06/16/1998	Shuman, S.	424	93.2	09/20/1996		
	AI2	5,776	,449	07/07/1998	Baum et al.	435	69.7	06/05/1995		
	AJ2	5,830	,707	11/03/1998	Bushman, F.D.	424	136.1	05/14/1996		
	AK2	5,837	,242	11/17/1998	Holliger et al.	424	130.1	00,11,		
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	AL2	WO 93	/15191	08/05/1993	WIPO			Ye		
	AM2	WO 93	/19172	09/30/1993	WIPO			Ye		
				02/17/1994	Canada			N		
	AN2	CA 2,	141,412	02/11/1994				Ye		
	A02	WO 94	4/17176	08/04/1994	WIPO			Ye		
	AP2	WO 97	7/06265	02/20/1997	WIPO			<u> </u>		
	17.12	1	OTHER	(Including Auth	or, Title, Date, Pertinen	nt Pages, etc.)				
	AR	2	Abremski, Topologica	K., <i>et al</i> ., "St lly Unlinked Pr	udies on the Properties o oducts Following Recombin	f P1 Site-Specifi ation," <i>Cell 32</i> :1	c Recombination 301-1311 (1993	n: Evidence for).		
	AS	2	Adams, D. from the	E., et al., "Co n Vitro Reactio	re-lox Recombination in Eson," J. Mol. Biol. 226:661	cherichia coli Ce -673 (1992).	lls: Mechanist	ic Differences		
	AT	2	Andrews, Target Se	B.J., et al., " quences," <i>Cell</i>	The FLP Recombinase of the 40:795-803 (1985).	e 2μ Circle DNA o	f Yeast: Inter	raction with It		
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Page 3 of 62

					ATTY. DOCKET NO. 0942.4640001	09/43	CATION NO. 8,358	
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<u>I</u>	NFORMAT 10	N DISCLO	OSURE STATEM	<u>IENT</u>	FILING DATE November 12, 1999	GROUP 1636		
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AMINER					NAME	CLASS	SUB-CLASS	FILING DATE
ITIAL			NT NUMBER	DATE	Devine, S.E., et al.	435	69.1	11/18/1994
	AA3	5,843,		12/01/1998	Elledge et al.	435	172.3	02/28/1997
	AB3	5,851,		12/22/1998	Winter et al.	435	6	06/07/1995
	AC3	5,858,		01/12/1999	Winter et al.	435	6	03/31/1994
	AD3	5,871,		02/16/1999	Szybalski, W.	435	91.1	11/21/1997
	AE3	5,874,		02/23/1999	Hartley et al.	435	6	06/07/1996
	AF3	5,888,		03/30/1999		435	325	04/17/1998
	AG3	5,916		06/29/1999	Bushman, F.D. Graham et al.	435	172.3	06/07/1995
	AH3	5,919		07/06/1999	Leboulch et al.	435	172.3	11/05/1996
	AI3	5,928		07/27/1999	Luo et al.	435	91.2	08/12/1997
	AJ3	5,989	,872	11/22/1999		435	69.7	05/29/1996
	AK3	6,010	,884	01/04/2000	Griffiths et al.			
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XAMINER		DOCUM	ENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
NITIAL				03/13/1997	WIPO			Y e
	AL3		7/09436		WIPO			Ye
	AM3		7/25446	07/17/1997	WIPO			Ye
	AN3	WO 97	7/32481	09/12/1997				Ye
	A03	WO 98	8/10086	03/12/1998	WIPO			Y
	AP3	WO 9	9/10488	03/04/1999	WIPO			
	AR	3			nor, Title, Date, Pertinent nteraction of the FLP Recor get Sequences," Mol. Cell. E	mhinase of the Sa	ccharomyces ce (1986).	erevisiae 2μm
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	ТА	3	Araki, H. 225:25-37	, et al., "Site (1992).	-specific Recombinase, R, E	Encoded by Yeast F	Plasmid pSR1,"	J. Mol. Biol.
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Page 4 of 62

					ATTY. DOCKET NO. 0942,4640001		APPL10 09/438	ATION NO. 3,358	
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	AS	4	Atlung, T.	, et al , "A vo	ersatile method for integ richia coli," Gene 107:11-	ration of ge -17 (1991).	enes and s	gene fusions	into the λ
	AT	4	Ausubel, Biology,	F.M., et al., " John Wiley & So	Maps of Plasmids pBR322 a ns, Inc., Boston, MA, (19	and pUC19,"	in Curren	t Protocols i	n Molecular
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					ATTY. DOCKET NO. APPLICATION NO. 0942.4640001 09/438,358				
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	AR	<u>5</u>	Augubal	M et al umus	agenesis by the Polymer John Wiley \$ Sons, Inc.	ase Chain re	eaction,"	in: Current 95). /	Protocols in
	AS	<u>5</u>	Babineau, 12391 (198	D. <i>et al.</i> , "The 15).	FLP Protein of the 2-mic	ro Plasmid o	of Yeast,"	J. Biol. Cf	nem. 260:12313-
	АТ	<u>5</u>	Balakrishr att-Int-me	man, R., et al., ediated rearrange	"A gene cassette for adament and $p_{ m L}$ expression v	apting <i>Eschei</i> ectors," <i>Ger</i>	richia col ne 138: 101	<i>i</i> strains as -104 (Januar	s hosts for y 1994).
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			OTHER	(Including Aut	nor, Title, Date, Pertinent	Pages, et	c.)		
	AR	6	Bayley, C site spec	.c., et al., "Exific recombinat	change of gene activity in ion system," Plant Mol. Bio	transgenio 1. 18:353-3	c plants 661 (199	catalyzed b	y the Cre- <i>lox</i>
	AS	6	Bethke, B stress ac 2834 (Jul	CIVALION OF CHA	, "Segmental genomic replain p53 promoter in single-co	cement by C py transfor	re-media	ated recombion Nucl. Acids	nation: genotox Res. 25: 2828 -
	AT	<u>6</u>	Bernard, DNA-topo	P., and Coutur	ier, M., "Cell Killing by t mplexes," <i>J. Mol. Biol. 226</i>	he F plasm :735-745 (1	id Ccdb 1992).	Protein Invo	lves Poisoning
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	AS	Z	Betz, U. recombina	A. K., et al. ation," Curr.	, "Bypass o Biol. 6:130	f lethality with 7-1316 (1996).	mosaic mi	ce genera	ted by Cre-10	oxP-mediated
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	AR	8	Black, L. lambda DN	W., "In vitro As," <i>Gene 46</i> :	packaging into phage 97-101 (1986).	T4 particles and	d specific	e recirculari	zation of phage
	AS	8	Bloch, C. Biochem.	A., et al., " Biophys. Res.	Purification of Escher Camm. 223:104-111 (199	ichia coli Chrom 96).	nosomal Se	egments witho	ut Cloning,"
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	ĀŤ	2	Brunelli, Designed 1 1318 (1993	for Directional	M. L., "A Series of Yeast Cloning of cDNAs and <i>cre/l</i>	:/Escherichia ox-Mediated	<i>coli 2</i> Plasmid	A Expression d Excision,"	Vectors Yeast 9:1309-

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	AS	10	Bubeck, P 21:3601-3	., et al., " 602 (1993).	'Rapid o	cloning by homologous	recombinat	ion <i>in viv</i>	o," Nucl. Act	ids Res.
	AT	10	Buchholz, targets i	F., et al., n genomic m	, "A sii anipula	mple assay to determin tion constructs," <i>Nucl</i>	ne the fund 1. Acids Re			P recombination 996).
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	AS	11	Bushman, 230:906-9	W., et al., "Co 11 (1985).	ontrol of Directionality	in Lambda Si	ite Specif	ic Recombina	tion," Science
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	AS	12	Chatterje artificie the endog	ee, P.K., and Con al chromosomes by genous and a tra	ren, J.S., "Isolating la y <i>in vivo</i> P1 packaging o nsposed <i>loxP</i> site," <i>Nucl</i>	rge nested do f products of Acids Res.	eletions f Cre-ca <i>25</i> :2205-	in bacteria talysed recon 2212 (June 1	l and P1 mbination between 997).
	AT	12	Craig, N	.L. and Nash, H. breakage of DNA	A., "The mechanism of ph by int topoisomerase,"	hage lambda s <i>Cell 35:795-</i>	ite-spec 803 (198	eific recombi 3).	nation: site-
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	AS	13	Dale, E. C. and Ow, D. W., "Intra- and intermolecular site-specific recombination in plant cells mediated by bacteriophage P1 recombinase," <i>Gene 91:79-85</i> (1990).								
	AT	13	Dale, E. host gend	C. and Ow, D.	W., "Gen tl. Acad.	e transfer with su Sci. USA 88:10558	ubsequent (-10562 (19	removal of 91).	the selection	on gene from the	
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	AS	14	Degryse, E constructi	., "In vivo int ons," <i>Gene 170</i> :	ermolecular recombinat 45-50 (1996).	ion in <i>Escher</i>	ichia coli	: applicatio	n to plasmid		
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	AS	18	Glasgow, A.C., et al., "DNA-binding Properties of the Hin Recombinase," J. Biol. Chem. 264: 10082 (1989).								
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INFORMATION DISCLOSURE STATEMENT

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	AT	21	Hoess, R. Recombina	H., et al., tion System,	Mechanism of Strand C J. Mol. Biol. 181:351	Leavage and Exchan	ge in t	he Cre- <i>lox</i> Si	te-specific
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	AS	<u>25</u>	Kozak, M. Acids Res	Kozak, M., "An analysis of 5'-noncoding sequences from 699 vertebrate messenger RNAs," Nucl. Acids Res. 15:8125-8132 (1987).								
	AT	<u>25</u>	Kozak, M. J. Biol.	, "Structural Chem. 266:1986	feat: 67-198	ures in eukaryotic mRNA 370 (1991).	s that mod	lulate the	e initiation	of translation,"		
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	AS	31	Medberry, recombine	S.L., et al	l., "In . Acids	tra-chromosomal rearran Res. 23:485-490 (1995)	ngements g	enerated b	y Cre- <i>lox</i> si	te-specific
	AT	31	Miki, T. DNA Gyra (1992).	et al., "Co se Subunit A	ntrol (ofS of Chromosomal DNA bess letD (ccdB) Product	by Sex Fac Growth I	ctor F in <i>l</i>	Escherichia c " J. Mol. Bi	oli. Mutants o
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	AS	32	Mizuuchi, attachmen	M. and Mizuu nt site of pha	uchi, K., "The extent of DNA se age lambda," <i>Nucl. Acids Res.</i> 1	equence requ 3:1193-1208	uired fo (1985).	r a functio	nal bacterial	
	AT	32	Mozo, T. Agrobacto	and Hooykaas erium-mediate	, P. J. J., "Design of a novel d plant transformation," Mol.	system for Gen. Genet 2	the con 236:1-7	nstruction (of vectors for	
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	AS	33	Nagaraja Bacterio	, R. and Weis phages HKO22	sberg, and λ	R. A., "Specificity De " J. Bacteriol 172:654	terminant 40-6550 (1	s in the A 1990).	ttachment Si	tes of
	AT	33	Nash, H. Sci. USA	A., "Integra 72:1072-1076	itive R 6 (197	ecombination of Bacteri	ophage La	mibda DNA i	In Vitro," P	roc. Natl. Acad.
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	AS	34	Nash, H. Enzymol.	A., "Purificati 100:210-216 (19	on and Properties of the 83).		age Lambd	a Int Protei	n," Meth.
	AT	34	Nash, H.	. A., et al., "Re e against joinin	ole of homology in site-s g of cohesive ends," <i>Proc</i>	specific rec c. Natl. Acad			iophage λ: 053 (1987).
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	AS	35	Nash, H.A Trends Bi	A., "Bending ochem. Sci 1	and sup 5:222-2	percoiling of DNA at t 27 (1990).	the attachm	ment site	of bacterioph	age lambda,"
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	AS	<u>38</u>	Padgett, PCR cloni	K. A. and Sor ing," <i>Gene 168</i>	ge, J. A., "Creat 1:31-35 (1996).	ing seamless jum	nctions i	ndependent	of rest	riction sites in		
	AT	38	Palazzol fusion-p	o, M. J., <i>et</i> rotein synthe	al., "Phage lambda sis and Cre-loxP a	a cDNA cloning v automatic plasmi	ectors fo d subclor	or subtract ning," <i>Gene</i>	ive hybi 88:25-3	ridization, 36 (1990).		
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	AR	<u>39</u>	Pan, G., 6 and Topois	et al., "Lig somerase I,"	gation o	of Synthetic Activated DN o1. Chem. 268(5):3683-368	MA Substr 9 (1993).	ates by S	ite-specific	Recombinases
	AS	39	Parks, R. Define a	J., and Gra Lower Limit	ham, f. for Ef	L., "A Helper-Dependent : ficient DNA Packaging," (System fo J. Virol.	or Adenovi 71(4):329	rus Vector P 93-3298 (Apri	roduction Helps il 1997).
	AT	39	Peakman, enzymatic	T. C., et a	1., "Hi	ghly efficient generatio e-specific <i>in vitro</i> recom				by 495-500 (1992).
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	AT	40	Pierce, bacterion (1992).	J. C., et al., 'phage P1 system	'A positive selection vect : Improved cloning efficac	or for cloni y," <i>Proc. Na</i>	ng high tl. Acad	molecular w . Sci. USA &	eight DNA by the 9:2056-2060	
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	AS	41	Pósfai, (i., et al., " Nucl. Acids	In viv Res. 2	o excision and amplific 2(12):2392-2398 (1994).	ation of	large segm	ents of the	Escherichia col
	AT	41	Prasad, of Mutat (1986).	P. V., et al	., "Su the Sy	ostrate Recognition by t	the 2μm Ci Minimal So	rcle Site ubstrate,"	Specific Red Mol. Cell. E	combinase: Effe 3101. 6:4329-433
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	AS	42	Reed, R.R 25:713-71	., "Transpose 9 (1981).	on-Mediated S	ite-Specific Rec	ombination	: A Defi	ned in Vitro	System," Cell
`	AT	42	Reed, R.F	R. and N.D. G and Protein-	rindley, "Tra DNA Linkage a	ansposon-Mediatec at the Recombinat	d Site-Spec tion Site,"	ific Reco Cell. 25	ombination in	n Vitro: DNA 081).
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	AS	44	Sauer, B Acad. Sc	., et al., "9 i. USA 84:910	Site-specific 08-9112 (1987)	insertion of DN	NA into a ps	eudorabie	s virus vec	tor," <i>Proc. Nat</i>
	AT	44	Sauer, E Sacchard	B., "Function Mnyces cerevi	nal Expression siae," Mol. Co	n of the cre-lox ell. Biol. 7:208	site-Speci 17-2096 (198	fic Recomb 7).	oination Sys	etem in the Yea
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	AS	46	Sauer, B. a natural	, "Multiplex and an engi	Cre/lox recombination per neered site in the yeast	rmits selecti genome," <i>Nucl</i>	ve site-s . Acids R	pecific DNA es. 24(23):46	targeting to bot 08-4613 (1996).		
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	AS	47	Schlake, Expressi	T., and Bode, on Cassettes at	J., "Use of Mutated FLP Defined Chromosomal Loc	Recognition Te ci," <i>Biochemist</i>	irget (FI <i>ry 33</i> :12	RT) Sites fo 1746-12751 (r the Exchange (
	AT	47	Segall, recombin	A. M. and Nash nation: integra	, H. A., "Synaptic inter se can align pairs of at				site-specific 576 (1993).
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	AS	48	Senecoff, Mutation	, J.F., et al., all Analysis of t	"DNA Recognition by the FLF the FLP Binding Site," J. Mo	P Recombinase of th	ne Yeast 2 μ 21 (1988).	Plasmid - A
	AT	48	Sheffiel of "para	d, P. et al., "C llel" expression	Overcoming expression and p n vectors," <i>Protein Expr.</i> I	urification proble Purific. 15:34-39 (ms of RhoGDI February 199	using a family 99).
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	AT	49	Smith, A	. J. H., et al.	, "A site-directed chromos bination," <i>Nat. Gen.</i> 9:376	somal translo 6-385 (1995).	ecation	induced in e	mbryonic stem
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	AS	<u>50</u>	Spengler Integrat	, S.J., et al., ive Recombinati	"The Stereostructure of on: Implications for Mech	Knots and Cat manism and DNA	enanes P Structu	roduced by ure," <i>Cell 4</i>	Phage λ 2: 32 5- 334 (198 5
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	AS	<u>53</u>	Tsurushit and light	a, N., et al., " chain genes to	Phage display vectors fo make large combinatorial	or in vivo r L libraries,	ecombinat " Gene 17	ion of immur 2:59-63 (199	oglobulin heav
	AT	53	Vanin, E. Mediated	F., et al., "De Recombination,"	velopment of High-Titer F J. Virol. 71:7820-7826 (Retroviral F (October 199	Producer (97).	Cell Lines b	y Using Cre-
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